BIOCHEMISTRY

SECOND EDITION

THE MOLECULAR BASIS

OF CELL STRUCTURE AND FUNCTION

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Table 11-7 Structures of some gangliosides†

	Symbol
NANA 2→3 Gal 1→4 Glc 1→ceramide	G_{Sn3}
GalNAc 1→4 Gal 1→4 Glc 1→ceramide 3 2 NANA	G_{M4}
3 GalNAc 1→4 Gal 1→4 Glc 1→ceramide 1 Gal 3 2 NANA	G_{M1}
3 GalNAc 1→4 Gal 1→4 Glc 1→ceramide 1 Gal 3 2 NANA NANA 2	G_{D1}
3 GalNAc 1→4 Gal 1→4 Glc 1→ceramide 1 Gal 3 2 NANA 8 NANA 2 NANA	G_{T1}

† Glc = D-glucose. Gal = D-galactose. GalNAc = N-acetyl-D-galactosamine. NANA = N-acetylneuramic acid (sialic acid). In this nomenclature of gangliosides, devised by L. Svennerholm, the subscript letters indicate the number of sialic acid groups (M = monosialo, D = disialo, and T = trisialo). The numeral in the subscript is $5 - n$, where n is the number of neutral sugar residues. The sialic acid residues are in color.

accumulates in the brain in Tay-Sachs disease, due to genetic lack of the enzyme required for its degradation (page 678). Several other genetic deficiency diseases result in abnormal accumulation of different glycosphingolipids (page 678).

Waxes

Waxes are water-insoluble, solid esters of higher fatty acids with long-chain monohydroxylic fatty alcohols or with sterols (see below). They are soft and pliable when warm but hard when cold. Waxes are found as protective coatings on skin, fur, and feathers, on leaves and fruits of higher plants, and on the exoskeleton of many insects. The major components of beeswax are palmitic acid esters of long-chain fatty alcohols with 26 to 34 carbon atoms. Lanolin, or wool fat, is a mixture of fatty acid esters of the sterols lanosterol and agnosterol (see below).

Simple (Nonsaponifiable) Lipids

The lipids discussed up to this point contain fatty acids as building blocks, which can be released on alkaline hydrolysis. The simple lipids contain no fatty acids. They occur in smaller amounts in cells and tissues than the complex lipids, but they include many substances having profound biological activity—vitamins, hormones, and other highly specialized fat-soluble biomolecules.

Handbook of PHARMACEUTICAL EXCIPIENTS

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Paraffin

1. Nonproprietary Names

BP: Hard paraffin
USPNF: Paraffin

2. Synonyms

905 (mineral hydrocarbons); hard wax; paraffinum durum; paraffinum solidum; paraffin wax.
See also Section 17.

3. Chemical Name and CAS Registry Number

Paraffin [8002-74-2]

4. Empirical Formula Molecular Weight

Paraffin is a purified mixture of solid saturated hydrocarbons having the general formula C_nH_{2n+2}, and is obtained from petroleum or shale oil.

5. Structural Formula

See Section 4.

6. Functional Category

Ointment base; stiffening agent.

7. Applications in Pharmaceutical Formulation or Technology

Paraffin is mainly used in topical pharmaceutical formulations as a component of creams and ointments. In ointments, it may be used to increase the melting point of a formulation or to add stiffness. Paraffin is additionally used as a coating agent for capsules and tablets and is used in some food applications.

8. Description

Paraffin is an odorless and tasteless, translucent, colorless or white solid. It feels slightly greasy to the touch and may show a brittle fracture. Microscopically, it is a mixture of bundles of microcrystals. Paraffin burns with a luminous, sooty flame. When melted, paraffin is essentially free from fluorescence in daylight; a slight odor may be apparent.

9. Pharmacopeial Specifications

Test	BP 1993	USPNF XVII
Identification	+	+
Congealing range	50–57°C	47–65°C
Reaction	—	+
Readily carbonizable substances	—	+
Sulfated ash	≤ 0.1%	—
Acidity or alkalinity	+	—

10. Typical Properties

Density: ≈ 0.84–0.89 g/cm^3 at 20°C
Melting point: various grades with different specified melting ranges are commercially available.
Solubility: soluble in chloroform, ether, volatile oils and most warm fixed oils; slightly soluble in ethanol; practically insoluble in acetone, ethanol (95%) and water. Paraffin can be mixed with most waxes if melted and cooled.

11. Stability and Storage Conditions

Paraffin is stable, although repeated melting and congealing may alter its physical properties. Paraffin should be stored at a temperature not exceeding 40°C in well-closed container.

12. Incompatibilities

–

13. Method of Manufacture

Paraffin is manufactured by the distillation of crude petroleum or shale oil, followed by purification by acid treatment and filtration. Paraffins with different properties may be produced by controlling the distillation and subsequent congealing conditions.
Synthetic paraffin, synthesized from carbon monoxide and hydrogen is also available, *see* Section 18.

14. Safety

Paraffin is generally regarded as an essentially nontoxic and nonirritant material when used in topical ointments and as a coating agent for tablets and capsules. However, granulomatous reactions (paraffinomas) may occur following injection of paraffin into tissue for cosmetic purposes or to relieve pain.[1–3]
See also Mineral Oil for further information.

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. In the UK, the recommended occupational exposure limits for paraffin wax fumes are 2 mg/m^3 long-term (8-hour TWA) and 6 mg/m^3 short-term.[4]

16. Regulatory Status

Accepted in the UK for use in certain food applications. Included in the FDA Inactive Ingredients Guide (oral capsules and tablets, topical emulsions, and ointments). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Aust, Br, Chin, Egypt, Fr, Ger, Hung, Ind, It, Jpn, Mex, Neth, Nord and USPNF. Also in BP Vet.
Note that the title paraffinum solidum, in certain pharmacopeias (Span, Swiss and Yug) refers to ceresin.

18. Related Substances

Ceresin; Light Mineral Oil; Microcrystalline Wax; Mineral Oil; Petrolatum; synthetic paraffin.

Ceresin
Comments: *see* Microcrystalline Wax.

Synthetic paraffin
Molecular weight: 400–1400
Pharmacopeias: USPNF.
Appearance: a hard, odorless, white wax consisting of a mixture of mostly long-chain, unbranched, saturated hydrocarbons along with a small amount of branched hydrocarbons.
Comments: the USPNF (Suppl 5) states that synthetic paraffin is synthesized by the Fischer-Tropsch process from carbon monoxide and hydrogen, which are catalytically converted to a mixture of paraffin hydrocarbons. The lower molecular weight fractions are removed by distillation and the residue is

hydrogenated and further treated by percolation through activated charcoal. This mixture may be fractionated into its components by a solvent separation method. Synthetic paraffin may contain not more than 0.005% of a suitable antioxidant.

19. Comments

The more highly purified waxes are used in preference to paraffin in many applications because of their specifically controlled physical properties such as, hardness, malleability and melting range.

20. Specific References

1. Crosbie RB, Kaufman HD. Self-inflicted oleogranuloma of breast. Br Med J 1967; 3: 840-841.
2. Bloem JJ, van der Waal I. Paraffinoma of the face: a diagnostic and therapeutic problem. Oral Surg 1974; 38: 675-680.
3. Greaney MG, Jackson PR. Oleogranuloma of the rectum produced by Lasonil ointment. Br Med J 1977; 2: 997-998.
4. Health and Safety Executive. EH40/93: occupational exposure limits 1993. London: HMSO. 1993.

21. General References

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22. Authors

USA: ZT Chowhan.

Anionic Emulsifying Wax

1. Nonproprietary Names

BP: Emulsifying wax

2. Synonyms

Collone HV; *Crodex A*; *Cyclonette Wax*; *Lanette wax SX BP*; *Polawax*.

3. Chemical Name and CAS Registry Number

Anionic emulsifying wax [8014-38-8]

4. Empirical Formula Molecular Weight

Anionic emulsifying wax contains cetostearyl alcohol, purified water, and either sodium lauryl sulfate or a sodium salt of a similar higher primary aliphatic alcohol. *See also* Sections 13 and 19.

5. Structural Formula

See Section 4.

6. Functional Categories

Emulsifying agent; stiffening agent.

7. Applications in Pharmaceutical Formulation or Technology

Anionic emulsifying wax is used in cosmetics and topical pharmaceutical formulations primarily as an emulsifying agent. The wax is added to fatty or paraffin bases to facilitate the production of oil-in-water emulsions which are nongreasy. In concentrations of about 2%, emulsions are pourable; stiffer emulsions, e.g. aqueous cream BP may contain up to 10% of anionic emulsifying wax.

Creams should be adequately preserved and can usually be sterilized by autoclaving. A better quality emulsion is produced by incorporating some alkali into the aqueous phase although care should be taken not to use an excess.

Anionic emulsifying wax (3-30%) may also be mixed with soft and liquid paraffins to prepare anhydrous ointment bases such as emulsifying ointment BP. A preparation of 80% anionic emulsifying wax in white soft paraffin has been used as a soap substitute in the treatment of eczema.

In addition, anionic emulsifying wax (10%) has been added to theobroma oil to produce a suppository base with a melting point of 34°C.

8. Description

An almost white, or pale yellow colored, waxy solid or flakes which when warmed become plastic before melting. Anionic emulsifying wax has a faint characteristic odor and a bland taste.

9. Pharmacopeial Specifications

Test	BP 1993
Identification	+
Acidity	+
Alkalinity	+
Alcohols	+
Iodine value	≤ 3.0
Saponification value	≤ 2.0
Sodium alkyl sulfates	≥ 8.7%
Unsaponifiable matter	≥ 86.0%
Water	≤ 4.0%

10. Typical Properties

Density: 0.97 g/cm^3
Flash point: > 100°C
Melting point: 52°C
Solubility: soluble in chloroform, ethanol (95%), ether and on warming in fixed oils and mineral oil; practically insoluble in water, forming an emulsion.

11. Stability and Storage Conditions

Solid anionic emulsifying wax is chemically stable and should be stored in a well-closed container in a cool, dry, place.

12. Incompatibilities

Incompatibilities of anionic emulsifying wax are essentially those of sodium alkyl sulfates and include: cationic compounds (quaternary ammonium compounds, acriflavine, ephedrine hydrochloride, antihistamines and other nitrogenous compounds); salts of polyvalent metals (aluminum, zinc, tin and lead); and thioglycollates. Anionic emulsifying wax is compatible with most acids above pH 2.5. It is also compatible with alkalis and hard water.

Iron vessels should not be used when heating anionic emulsifying wax; stainless steel containers are satisfactory.

13. Method of Manufacture

Anionic emulsifying wax is prepared by melting cetostearyl alcohol and heating to about 95°C. Sodium lauryl sulfate, or some other suitable anionic surfactant, and purified water is then added. The mixture is heated to 115°C and while this temperature is maintained the mixture is vigorously stirred until any frothing ceases. The wax is then rapidly cooled.

The BP 1993 specifies that the formula of anionic emulsifying wax is:

Cetostearyl alcohol 90 g
Sodium lauryl sulfate 10 g
Purified water 4 mL

14. Safety

Anionic emulsifying wax is used primarily in topical pharmaceutical formulations and is generally regarded as a nontoxic and nonirritant material. However, sodium lauryl sulfate, a constituent of anionic emulsifying wax, is known to be irritant to the skin at high concentrations; sodium cetyl sulfate is claimed to be less irritating.

Emulsifying ointment BP, which contains anionic emulsifying wax, has been found to have major sunscreen activity in clinically normal skin and should therefore not be used before phototherapy procedures.[1]

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection is recommended.

16. Regulatory Status

Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Belg, Br, Ger, Ind, Nord, Swiss and Yug.
Note that the Belgian Pharmacopeia includes anionic emulsifying wax prepared from 9 parts cetostearyl alcohol and 1 part sodium cetostearyl sulfate. The German Pharmacopeia includes anionic emulsifying wax prepared from 12.5 parts cetostearyl alcohol and 1 part sodium cetostearyl sulfate.

18. Related Substances

Cetostearyl alcohol; Nonionic Emulsifying Wax; Sodium Lauryl Sulfate.
A number of emulsifying waxes are commercially available which contain different sodium alkyl sulfates and may not meet official compendial specifications. *See also* Section 19.

19. Comments

The nomenclature for emulsifying wax is confused since there are three groups of emulsifying waxes with different titles in the UK and US:

	UK	US
Nonionic	Cetomacrogol emulsifying wax	Emulsifying wax
Anionic	Emulsifying wax	—
Cationic	Cetrimide emulsifying wax	—

Each wax has similar physical properties, but varies in the type of surfactant used which, in turn, affects the range of compatibilities. Emulsifying wax BP and emulsifying wax USPNF contain anionic and nonionic surfactants respectively and are therefore not interchangeable in formulations.

20. Specific References

1. Cox NH, Sharpe G. Emollients, salicylic acid, and ultraviolet erythema [letter]. Lancet 1990; 335: 53-54.

21. General References

Eccleston GM. Properties of fatty alcohol mixed emulsifiers and emulsifying waxes. In: Florence AT, editor. Materials used in pharmaceutical formulation: critical reports on applied chemistry, volume 6. Oxford: Blackwell Scientific Publications, 1984: 124-156.

22. Authors

UK: AJ Winfield.

Carnauba Wax

1. Nonproprietary Names

BP: Carnauba wax
PhEur: Cera carnauba
USPNF: Carnauba wax

2. Synonyms

903; brazil wax; caranda wax.

3. Chemical Name and CAS Registry Number

Carnauba wax [8015-86-9]

4. Empirical Formula Molecular Weight

Carnauba wax consists primarily of a complex mixture of esters of acids and hydroxyacids. Also present are acids, oxypolyhydric alcohols, hydrocarbons, resinous matter and water.

5. Structural Formula

See Section 4.

6. Functional Category

Coating agent.

7. Applications in Pharmaceutical Formulation or Technology

Carnauba wax is widely used in cosmetics, certain foods and pharmaceutical formulations.
Carnauba wax is the hardest and highest melting of the waxes commonly used in pharmaceutical formulations and is used primarily as a 10% w/v aqueous emulsion to polish sugar-coated tablets. Aqueous emulsions may be prepared by mixing carnauba wax with an ethanolamine compound and oleic acid. The carnauba wax coating produces tablets of good luster without rubbing. Carnauba wax may also be used in powder form to polish sugar-coated tablets.
Carnauba wax (10-50% w/w) has also been used alone or with stearyl alcohol to produce sustained release solid dosage formulations.[1-4]

8. Description

Carnauba wax occurs as a light brown to pale yellow colored powder, flakes, or irregular lumps of a hard, brittle wax. It possesses a characteristic bland odor and practically no taste. It is free from rancidity. Commercially, various types and grades are available.

9. Pharmacopeial Specifications

Test	PhEur 1989	USPNF XVII
Identification	+	—
Appearance of solution	+	—
Melting range	80-88°C	81-86°C
Residue on ignition	—	≤ 0.25%
Total ash	≤ 0.25%	—
Heavy metals	—	≤ 0.004%
Acid value	2-7	2-7
Saponification value	78-95	78-95

10. Typical Properties

Flash point: 270-330°C
Refractive index: $n_D^{80} = 1.450$
Solubility: soluble in warm chloroform, and warm toluene; slightly soluble in boiling ethanol (95%); practically insoluble in water.
Specific gravity: 0.990-0.999 at 25°C
Unsaponified matter: 50-55%

11. Stability and Storage Conditions

Carnauba wax is stable and should be stored in a well-closed container, in a cool, dry, place.

12. Incompatibilities

–

13. Method of Manufacture

Carnauba wax is obtained from the leaf buds and leaves of *Copernicia cerifera* Mart. (Fam. Palmae). The leaves are dried and shredded and the wax then removed by the addition of hot water.

14. Safety

Carnauba wax is widely used in oral pharmaceutical formulations, cosmetics, and certain food products and is generally regarded as an essentially nontoxic and nonirritant material.

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16. Regulatory Status

GRAS listed. Accepted for use in certain foods in the UK. Included in the FDA Inactive Ingredients Guide (oral capsules and tablets, also topical preparations). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Br, Eur, Fr, Ger, Jpn, Neth, Swiss and USPNF.

18. Related Substances

–

19. Comments

In cosmetics, carnauba wax is mainly used to increase the stiffness of formulations, e.g. lipsticks and mascaras.

20. Specific References

1. Wiseman EH, Federici NJ. Development of a sustained-release aspirin tablet. J Pharm Sci 1968; 51: 1535-1539.
2. Prasad CM, Srivastava GP. Study of some sustained release granulations of aspirin. Indian J Hosp Pharm 1971; 8: 21-28.
3. Dave SC, Chakrabarti T, Srivastava GP. Sustained release tablet formulation of diphenhydramine hydrochloride (Benadryl) - part II. Indian J Pharm 1974; 36: 94-96.
4. Kumar K, Chakrabarti T, Srivastava GP. Sustained release tablet formulation of diethylcarbamazine citrate (Hetrazan). Indian J Pharm 1975; 37: 57-59.

21. General References

Briquet F, Brossard C, Ser J, Duchêne D. Optimization of a sustained release formulation containing spherical microgranules produced

by extrusion-spheronization [in French]. STP Pharma 1986; 2: 986-994.

22. Authors

USA: NH Kobayashi.

Microcrystalline Wax

1. Nonproprietary Names

USPNF: Microcrystalline wax

2. Synonyms

Amorphous wax; petroleum ceresin; petroleum wax (microcrystalline).

3. Chemical Name and CAS Registry Number

Microcrystalline wax [63231-60-7]

4. Empirical Formula Molecular Weight

Microcrystalline wax is composed of a mixture of straight-chain and randomly branched saturated alkanes obtained from petroleum. The carbon chain lengths range from C_{41}-C_{57}; cyclic hydrocarbons are also present.

5. Structural Formula

See Section 4.

6. Functional Category

Coating agent; stiffening agent.

7. Applications in Pharmaceutical Formulation or Technology

Microcrystalline wax is used mainly as a stiffening agent in topical creams and ointments. The wax is used to modify the crystal structure of other waxes (particularly paraffin wax) present in a mixture so that changes in crystal structure, usually exhibited over a period of time, do not occur. Microcrystalline wax also minimizes the sweating or bleeding of oils from blends of oils and waxes. Microcrystalline wax generally has a higher melting point and higher viscosity when molten, thereby increasing the consistency of creams and ointments when incorporated.

Microcrystalline wax is also used as a tablet and capsule coating agent, and in confectionery, cosmetics and food products.

8. Description

Microcrystalline wax occurs as odorless and tasteless waxy lumps or flakes containing small irregularly shaped crystals. It may vary in color from white to yellow, amber, brown or black depending on the grade of material; pharmaceutical grades are usually white or yellow-colored.

9. Pharmacopeial Specifications

Test	USPNF XVII
Color	+
Melting range	54-102°C
Consistency	3-100
Acidity	+
Alkalinity	+
Residue on ignition	≤ 0.1%
Organic acids	+
Fixed oils, fats, and rosin	+

10. Typical Properties

Acid value: 1.0

Density: 0.928-0.941 g/cm^3

Freezing point: 60-75°C

Refractive index: n_D^{100} = 1.435-1.445

Saponification value: 0.05-0.10

Solubility: soluble in benzene, chloroform and ether; slightly soluble in ethanol; practically insoluble in water. When melted, microcrystalline wax is miscible with volatile oils and most warm fixed oils. *See also* HPE Data.

Viscosity (dynamic):
10-30 mPa s (10-30 cP) at 100°C.

	HPE Laboratory Project Data		
	Method	Lab #	Results
Solubility			
Ethanol (95%) at 25°C	SOL-4	10	0.003 mg/mL
Ethanol (95%) at 37°C	SOL-4	10	0.003 mg/mL
Hexane at 25°C	SOL-4	10	0.053 mg/mL
Hexane at 37°C	SOL-4	10	0.088 mg/mL
Propylene glycol at 25°C	SOL-4	10	0.001 mg/mL

Supplier: International Wax Refining Co.

11. Stability and Storage Conditions

Microcrystalline wax is stable in the presence of acids, alkalis, light and air. The bulk material should be stored in a well-closed container in a cool, dry, place.

12. Incompatibilities

-

13. Method of Manufacture

Microcrystalline wax is obtained by solvent fractionation of the still bottom fraction of petroleum by suitable dewaxing or de-oiling.

14. Safety

Microcrystalline wax is mainly used in topical pharmaceutical formulations but is also used in some oral products. It is generally regarded as a nontoxic and nonirritating material.

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection is recommended.

16. Regulatory Status

GRAS listed. Included in the FDA Inactive Ingredients Guide (oral capsules and topical preparations). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Swiss and USPNF.

18. Related Substances

Ceresin; Paraffin.

Ceresin

Pharmacopeias: Swiss and Yug.

Comments: ceresin is a mixture of solid hydrocarbons obtained by the purification of ozokerite, a naturally occuring solid paraffin.

19. Comments
–

20. Specific References
–

21. General References
–

22. Authors
USA: LD Bighley.

Nonionic Emulsifying Wax

1. Nonproprietary Name

BP: Cetomacrogol emulsifying wax
USPNF: Emulsifying wax

2. Synonyms

Collone NI; Crodex N; Ritachol; T-Wax.

3. Chemical Name and CAS Registry Number

Nonionic emulsifying wax [977069-99-0]

4. Empirical Formula Molecular Weight

The USPNF XVII describes nonionic emulsifying wax as emulsifying wax, prepared from cetostearyl alcohol and containing a polyoxyethylene derivative of a fatty acid ester of sorbitan. However, the BP 1993 describes nonionic emulsifying wax as cetomacrogol emulsifying wax prepared from cetostearyl alcohol and cetomacrogol 1000. The UK and US materials may therefore be constitutionally different. *See also* Section 19.

5. Structural Formula

See Section 4.

6. Functional Category

Emulsifying agent; stiffening agent.

7. Applications in Pharmaceutical Formulation or Technology

Nonionic emulsifying wax is used as an emulsifying agent in the production of oil-in-water emulsions which are unaffected by moderate concentrations of electrolytes and are stable over a wide pH range. The concentration of wax used alters the consistency of a product due to its 'self-bodying action'; at concentrations up to about 5% a product is pourable.
Concentrations of about 15% of nonionic emulsifying wax are commonly used in creams, but concentrations as high as 25% may be employed, e.g. in chlorhexidine cream BP. Nonionic emulsifying wax is particularly recommended for use with salts of polyvalent metals and medicaments based on nitrogenous compounds. Creams are susceptible to microbial spoilage and should be adequately preserved.
Nonionic emulsifying wax is also used in nonaqueous ointment bases, such as cetomacrogol emulsifying ointment BP and in barrier creams.

8. Description

Nonionic emulsifying wax is a white or off-white colored waxy solid or flakes which melt when heated to give a clear, almost colorless liquid. Nonionic emulsifying wax has a faint odor characteristic of cetostearyl alcohol.

9. Pharmacopeial Specifications

Test	BP 1993	USPNF XVII (Suppl 7)
Identification	+	—
Melting range	—	50–54°C
Solidifying point	45–53°C	—
pH (3% dispersion)	—	5.5–7.0
Alkalinity	+	—
Acid value	≤ 0.5	—
Hydroxyl value	175–192	178–192
Iodine value	—	≤ 3.5
Refractive index (at 60°C)	1.435–1.439	—
Saponification value	≤ 2.0	≤ 14.0

10. Typical Properties

Density: 0.94 g/cm^3
Flash point: > 55°C
Solubility: freely soluble in aerosol propellants, chloroform, ether, and hydrocarbons; soluble in ethanol (95%); insoluble in water (forms emulsions).

11. Stability and Storage Conditions

Nonionic emulsifying wax is stable and should be stored in a well-closed container in a cool, dry, place.

12. Incompatibilities

Nonionic emulsifying wax is incompatible with tannin, phenol and phenolic materials, resorcinol and benzocaine. It may reduce the antibacterial efficacy of quaternary ammonium compounds.

13. Method of Manufacture

The BP 1993 specifies that cetomacrogol emulsifying wax (nonionic emulsifying wax) may be prepared by melting and mixing together 80 g of cetostearyl alcohol and 20 g of cetomacrogol 1000. The mixture is then stirred until cold.
The USPNF XVII formula for nonionic emulsifying wax is a mixture of unstated proportions of cetostearyl alcohol and a polyoxyethylene derivative of a fatty acid ester of sorbitan.

14. Safety

Nonionic emulsifying wax is used in cosmetics and topical pharmaceutical formulations and is generally regarded as a nontoxic and nonirritant material.

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled. Eye protection is recommended.

16. Regulatory Status

Included in the FDA Inactive Ingredients Guide (topical aerosols, emulsions, lotions and ointments). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Br and USPNF. Also in BP Vet.

18. Related Substances

Anionic Emulsifying Wax; cationic emulsifying wax; Cetostearyl Alcohol; Polyoxyethylene Alkyl Ethers.

It should be noted that there are many similar nonionic emulsifying waxes composed of different nonionic surfactants and fatty alcohols.

Cationic emulsifying wax

Synonyms: cetrimide emulsifying wax; *Crodex C*.

Method of manufacture: cetrimide emulsifying wax is prepared similarly to nonionic emulsifying wax and contains 90 g of cetostearyl alcohol and 10 g of cetrimide.

Comments: cationic emulsifying wax is claimed to be of particular value in cosmetic and pharmaceutical formulations when cationic characteristics are important. Thus it can be used in medicated creams, germicidal creams, ointments and lotions, hair conditioners, baby creams and skin care products in which cationic compounds are included. Cationic emulsifying wax is compatible with cationic and nonionic materials, but is incompatible with anionic surfactants and drugs. Additional antimicrobial preservatives should be included in creams. Cetrimide may cause irritation to the eye, *see* Cetrimide.

19. Comments

The nomenclature for emulsifying wax is confused since there are three groups of emulsifying waxes with different titles in the UK and US:

	UK	US
Nonionic	Cetomacrogol emulsifying wax	Emulsifying wax
Anionic	Emulsifying wax	—
Cationic	Cetrimide emulsifying wax	—

Each wax has similar physical properties, but varies in the type of surfactant used which, in turn, affects the range of compatibilities. Emulsifying wax BP and emulsifying wax USPNF contain anionic and nonionic surfactants respectively and are therefore not interchangeable in formulations.

20. Specific References

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21. General References

Eccleston GM. Properties of fatty alcohol mixed emulsifiers and emulsifying waxes. In: Florence AT, editor. Materials used in pharmaceutical formulation: critical reports on applied chemistry, volume 6. Oxford: Blackwell Scientific Publications, 1984: 124-156.

Hadgraft JW. The emulsifying properties of polyethyleneglycol ethers of cetostearyl alcohol. J Pharm Pharmacol 1954; 6: 816-829.

22. Authors

UK: AJ Winfield.

White Wax

1. Nonproprietary Names

BP: White beeswax
PhEur: Cera alba
USPNF: White wax

2. Synonyms

Bleached wax; E901.

3. Chemical Name and CAS Registry Number

White beeswax [8012-89-3]

4. Empirical Formula Molecular Weight

White wax is the chemically bleached form of natural beeswax, *see* Section 13.
Beeswax consists of 70–75% of a mixture of various esters of straight chain monohydric alcohols with even number carbon chains from C_{24}-C_{36} esterified with straight chain acids which also have even numbers of carbon atoms up to C_{36} together with some C_{18} hydroxy acids. The chief ester is myricyl palmitate. Also present are free acids (about 14%) and carbohydrates (about 12%) as well as approximately 1% free wax alcohols and stearic esters of fatty acids.

5. Structural Formula

See Section 4.

6. Functional Category

Emulsion stabilizer; stiffening agent.

7. Applications in Pharmaceutical Formulation or Technology

White wax is a chemically bleached form of yellow wax and is used in similar applications, such as to increase the consistency of creams and ointments, and to stabilize water-in-oil emulsions. White wax is also used to polish sugar-coated tablets and to adjust the melting point of suppositories.
See also Yellow Wax.

8. Description

White wax consists of tasteless, white or slightly yellow-colored sheets or fine granules with some translucence. Odor is similar to yellow wax although it is less intense.

9. Pharmacopeial Specifications

Test	PhEur 1981	USPNF XVII
Melting range	61–65°C	62–65°C
Saponification cloud test	—	+
Saponification value	87–104	—
Fats, or fatty acids, Japan wax, rosin and soap	—	+
Acid value	17–24	17–24
Ester value	70–80	72–79
Ratio number	3.3–4.3	—
Ceresin, paraffin and certain other waxes	+	—
Glycerin and other polyhydric alcohols	≤ 0.5%	—

10. Typical Properties

Arsenic: ≤ 3 ppm
Density: 0.95–0.96 g/cm^3
Flash point: 245–258°C
Heavy metals: ≤ 0.004%
Iodine number: 8–11
Lead: ≤ 10 ppm
Melting point: 61–65°C
Peroxide value: ≤ 8
Solubility: soluble in chloroform, ether, fixed oils, volatile oils and warm carbon disulfide; sparingly soluble in ethanol (95%); practically insoluble in water.
Unsaponified matter: 52–55%

	HPE Laboratory Project Data		
	Method	Lab #	Results
Density	DE-1	7	0.958 ± 0.006 g/cm^3

11. Stability and Storage Conditions

When heated above 150°C esterification occurs with a consequent lowering of acid value and elevation of melting point. White wax is stable when stored in a well-closed container, protected from light.

12. Incompatibilities

Incompatible with oxidizing agents.

13. Method of Manufacture

Beeswax (yellow wax) is obtained from the honeycomb of the bee [*Apis mellifera* Linné (Fam. Apidae)], *see* Yellow Wax. Subsequent treatment with oxidizing agents bleaches the wax to yield white wax.

14. Safety

Used in both topical and oral formulations, white wax is generally regarded as being an essentially nontoxic and nonirritant material. However, although rare, hypersensitivity reactions to beeswax, attributed to contaminants in the wax, have been reported.[1,2]

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16. Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (oral capsules and tablets, rectal, topical and vaginal preparations). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Aust, Belg, Br, Cz, Egypt, Eur, Fr, Ger, Gr, Hung, Ind, It, Jpn, Mex, Neth, Nord, Port, Rom, Swiss, USPNF and Yug. Also in BP Vet.

18. Related Substances

Yellow Wax.

19. Comments

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20. Specific References

1. Cronin E. Contact dermatitis from cosmetics. J Soc Cosmet Chem 1967; 18: 681-691.
2. Rothenborg HW. Occupational dermatitis in beekeeper due to poplar resins in beeswax. Arch Dermatol 1967; 95: 381-384.

21. General References

Puleo SL. Beeswax. Cosmet Toilet 1987; 102(6): 57-58.

22. Authors

USA: LD Bighley.

Yellow Wax

1. Nonproprietary Names

BP: Yellow beeswax
PhEur: Cera flava
USPNF: Yellow wax

2. Synonyms

E901; refined wax.

3. Chemical Name and CAS Registry Number

Yellow beeswax [8012-89-3]

4. Empirical Formula Molecular Weight

Yellow wax is naturally obtained beeswax, *see* Section 13. Beeswax consists of 70-75% of a mixture of various esters of straight chain monohydric alcohols with even number carbon chains from C_{24}-C_{36} esterified with straight chain acids which also have even numbers of carbon atoms up to C_{36} together with some C_{16} hydroxy acids. The chief ester is myricyl palmitate. Also present are free acids (about 14%) and carbohydrates (about 12%) as well as approximately 1% free wax alcohols and stearic esters of fatty acids.

5. Structural Formula

See Section 4.

6. Functional Category

Emulsion stabilizer; stiffening agent.

7. Applications in Pharmaceutical Formulation or Technology

Yellow wax is used in food, cosmetics and confectionery products. However, its main use is in topical pharmaceutical formulations, where it is used at a concentration of 5-20%, as a stiffening agent in ointments and creams. Yellow wax is also employed in emulsions since it enables water to be incorporated into water-in-oil emulsions.
In some oral formulations, yellow wax is used as a polishing agent for sugar-coated tablets; it is also used in sustained release formulations.
Yellow wax forms a soap with borax.

8. Description

Yellow or light brown pieces or plates with a fine-grained matt, noncrystalline fracture and a faint characteristic odor. The wax becomes soft and pliable when warmed.

9. Pharmacopeial Specifications

Test	PhEur 1981	USPNF XVII
Melting range	61-65°C	62-65°C
Saponification cloud test	—	+
Saponification value	87-102	—
Fats, or fatty acids, Japan wax, rosin and soap	—	+
Acid value	17-22	17-24
Ester value	70-80	72-79
Ratio number	3.3-4.3	—
Ceresin, paraffin and certain other waxes	+	—
Glycerin and other polyhydric alcohols	≤ 0.5%	—

10. Typical Properties

Acid value: 20
Arsenic: ≤ 3 ppm
Density: 0.950-0.960 g/cm^3
Flash point: 245-258°C
Heavy metals: ≤ 0.004%
Iodine number: 8-11
Lead: ≤ 10 ppm
Melting point: 61-65°C
Peroxide value: ≤ 8
Refractive index: 1.440-1.445
Solubility: soluble in chloroform, ether, fixed oils, volatile oils, and warm carbon disulfide; sparingly soluble in ethanol (95%); practically insoluble in water.
Unsaponified matter: 52-55%
Viscosity (kinematic):
1470 mm^2/s (1470 cSt) at 99°C

11. Stability and Storage Conditions

When heated above 150°C esterification occurs with a consequent lowering of acid value and elevation of melting point. Yellow wax is stable when stored in a well-closed container, protected from light.

12. Incompatibilities

Incompatible with oxidizing agents.

13. Method of Manufacture

Yellow wax is a natural secretion of bees [*Apis mellifera* Linné (Fam. Apidae)] and is obtained commercially from honeycombs. Honey is abstracted from combs either by draining or centrifugation and water added to the remaining wax to remove soluble impurities. Hot water is then added to form a floating melt which is strained to remove foreign matter. The wax is then poured into flat dishes or molds to cool and harden.

14. Safety

Used in both topical and oral formulations, yellow wax is generally regarded as being an essentially nontoxic and nonirritant material. However, hypersensitivity reactions attributed to contaminants in the wax, although rare, have been reported.[1,2]

15. Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16. Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (oral capsules and tablets, and topical preparations). Included in nonparenteral medicines licensed in the UK.

17. Pharmacopeias

Aust, Belg, Br, Chin, Egypt, Eur, Fr, Ger, Ind, It, Jpn, Neth, Nord, Port, Rom, Swiss, USPNF and Yug.

18. Related Substances

White Wax.

19. Comments

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20. Specific References

1. Cronin E. Contact dermatitis from cosmetics. J Soc Cosmet Chem 1967; 18: 681-691.
2. Rothenborg HW. Occupational dermatitis in beekeeper due to poplar resins in beeswax. Arch Dermatol 1967; 95: 381-384.

21. General References

Pulco SL. Beeswax. Cosmet Toilet 1987; 102(6): 57-58.

22. Authors

USA: LD Bighley.